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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MCHALE & SLAVIN, P.A.
2855 PGA BLVD
PALM BEACH GARDENS, FL 33410

EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,796	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1, 39, 40, 42 and 44 have been amended as requested in the amendment filed on February 09, 2006. Following the amendment, claims 1 and 39-46 are pending in the instant application.

Claims 39-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made by original presentation (Paper mailed on March 09, 2004).

Claim 1 is under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on February 09, 2006 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

6. Claims 1 stands rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for reasons of record fully explained in the previous office communications.

Claim 1, as currently presented, is directed to a biopolymer marker consisting of SEQ ID NO: 1 or SEQ ID NO: 4 which evidences a link to Type II diabetes. The instant specification

provides a disclosure of a protocol, under which samples of blood collected from diabetes patients, age-matched controls and pooled control samples were analyzed by using mass spectrometric and chromatographic techniques. The results of the analysis are presented in Figures 1-8 and also within the text of the instant specification. Specifically, finding of the "disease specific marker" identified by an amino acid sequence is presented at page 46 of the instant specification. At bottom of page 46 continuing to page 47, Figures 1 and 3 are described as "photographs of a gel which is indicative of the presence/absence of the marker in disease vs. control and, in cases where the marker is always present, the relative strength, e.g. the up or down regulation of the marker relative to categorization of diseases state is deduced". Brief description of the figures (page 37) does not contain any disclosure of how biopolymer markers of SEQ ID NO: 1 or SEQ ID NO: 4 correspond to the bands as shown in Figures. Because the instant specification at the time of filing fails to disclose any meaningful information regarding specific association of peptide of SEQ ID NO: 1 or SEQ ID NO: 4 and Type II diabetes, the Examiner maintains that based on the information presented, the instant claimed invention, an isolated biopolymer marker of SEQ ID NO: 1 or SEQ ID NO: 4, asserted to be useful for diagnostics and therapeutics for Type II diabetes, clearly lacks specific and substantial credible real-world utility and, therefore, the instant invention does not meet the requirements of 35 U.S.C. 101.

Applicant traverses the instant rejection on the premises that:

1) the Examiner's statements are contradictory and reveal an incomplete understanding of the invention (pages 9-15 of the Response);

2) the instant specification presents a clear and unambiguous definition of "biopolymer marker which evidences a link to Type II diabetes" (pages 16-21);

3) the specific and substantial credible utility of the claimed biopolymer marker for diagnostics and/or therapeutics of Type II diabetes is based on the showing of "differential expression" of the markers of SEQ ID NO: 1 and SEQ ID NO: 4 between samples obtained from diabetes patients and age matched normal control (pages 9-12 and 22-36).

Applicant's arguments have been fully considered but are not persuasive for the following reasons.

1) Applicant submits that "the instant inventors identified the claimed peptides (SEQ ID NO: 1 and 4) as markers for type II diabetes by carrying out the disclosed methods. These identified markers can then be used as markers for Type II diabetes, i.e. by testing unknown samples for the presence of the markers or alternatively the disclosed methods can be used to identify markers in another disease condition" (pages 9-10 of the Response). Applicant further explains that " [o]ne of ordinary skill in the art would be able to determine the nature of this relationship from simple observation of a gel such as shown in Figure 1; for example, in the instant case, the claimed peptides are present in normal samples and absent in Type II diabetes however in another disease condition a marker may be present in the disease and absent in the normal or present in both disease an normal at different levels" (pages 10-11). Thus, it appears that in order to use the claimed biopolymer markers of SEQ ID NO: 1 or 4 for any diagnostic or therapeutic purposes, a skilled practitioner first has to establish the meaning of finding of the peptide of SEQ ID NO: 1 or 4 in a sample obtained from a patient. Because the instant specification fails to present any meaningful information regarding the association of the claimed

peptides of SEQ D NO: 1 or 4 with Type II diabetes, one would reasonably conclude that the instant claimed markers cannot be immediately useful as a diagnostic tools for diabetes. While an assay that detects the presence of a marker that has a stated correlation to a specific disease would be considered as a "substantial utility" in the context of being useful for diagnosis, in the instant case the disclosure "that the claimed markers (SEQ ID NO: 1 and 4) are present in normal patients [...] but are not strongly present in Type II diabetes patients" (page 14-15, emphasis added) is clearly not sufficient to establish their utility.

The Court in *Brenner v. Manson* held that "[t]he basic *pro quid quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point – where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

§101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form *Brenner*, 383, U.S. at 534-35, 148 USPQ at 695. *Brenner's* standard has been interpreted to mean that "vague, general disclosures or arguments of "useful in research" or "useful as building blocks of value to the researcher" would not satisfy §101. See *Kirk*, 376 F. 2d at 945 153 USPQ at 55 (interpreting *Brenner*).

2) The instant specification presents several definitions of a "biopolymer marker" (see pages 5, 6 especially 11 and 21), essentially that it is a polymer of biological origin (bottom at page 21), which can be present/absent/down-regulated/upregulated with respect to a disease condition (page11). However, according to Webster dictionary "a marker" is "one that marks or

distinguishes". The instant invention is based on finding that peptides of SEQ ID NO: 1 or SEQ ID NO: 4 are differentially present in patients with Type II diabetes as compared to control normal individuals. There appears to be no further information presented in the instant specification as to what constitutes finding of a peptide of SEQ ID NO: 1 or SEQ ID NO: 4 in a sample. For example, if a peptide of SEQ ID NO: 1 was found in a sample obtained from a patient and "the link to Type II diabetes" was identified, would that mean that a patient has Type II diabetes or is at risk to develop the disease? The instant specification fails to provide any factual evidence that finding of a peptide of SEQ ID NO: 1 could lead to any meaningful determination for a "link" to Type II diabetes or would be useful for diagnosis or treatment of Type II diabetes, as asserted by Applicant. Thus, in order to practice the claimed invention, a skilled artisan would have to engage in a substantial amount of further research to establish the utility of the claimed peptides of SEQ ID NO: 1 or 4 in the diagnosis of Type II diabetes. Finally, by Applicant's own admission, since "[t]he claimed biopolymer markers (SEQ ID NO: 1 and 4) [are] not specifically diagnostic of any condition" (page 16), their asserted utility as diagnostic tools for Type II diabetes appears to be not substantiated by any evidence of record.

At page 18 of the Response, Applicant argues that "even if the only information obtained from identifying the presence of a marker SEQ ID NO: 1 or of SEQ ID NO: 4 is the determination of a link to Type II diabetes, [...] such information would be enough to establish the utility of the instant invention since the showing of a link between the claimed peptides (SEQ ID NO: 1 and SEQ ID NO: 5) and Type II diabetes implies the potential for use of the claimed peptides for diagnosis and/or therapeutics for Type II diabetes". Applicant's attention is directed to the decision of *Brenner v. Manson* , in which the Supreme Court held that the grant of patent

rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure that justifies granting him the right to exclude others. See *Brenner* 383 U.S. at 534, 148 USPQ at 695. Thus, the basis *quid pro quo* of the patent system is the grant of a valuable legal right in exchange for a meaningful disclosure of the claimed invention. In the instant case, the general suggestions for potential use of the disclosed products do not entitle Applicant to the legal right they claim to exclude others from using those products.

Applicant argues that "[t]he data presented in Figures 1 and 3 [...] clearly evidences that the claimed biopolymer markers (SEQ ID NO: 1 and 4) were found to be differentially expressed between Type II diabetes patients and patients determined to be normal with regard to Type II diabetes. Thus, Applicants assert that the claimed biopolymer markers (SEQ ID NO: and 4) are useful for diagnosis and treatment of Type II diabetes (an "asserted utility")" (pages 20-21 of the Response). However, the record does not support Applicant's position that the characterization of a peptide as being "differentially expressed" or ""not strongly present" would have suggested a basis for patentable utility as a diagnostic marker to a person skilled in the art at the time the application was filed in view of the total absence of disclosure of what constitutes the finding of the claimed marker in a sample. In the terms used by the *Brenner* Court, such a characterization does not provide a specific utility in currently available form.

3) At pages 22-26 of the Response, Applicant argues that "the Examiner apparently believes that differential expression is an insignificant observation to consider wheh evaluating a peptide as a potential marker" (page 22) and further that "that a marker can only be a peptide found in a

disease state and not found in a normal physiological state" (page 26). However, Applicant mischaracterizes the Examiner's position. To clarify, the Examiner has never disputed that the instant peptides of SEQ ID NO: 1 or SEQ ID NO: 4 could be differentially expressed in the samples of patients with Type II diabetes. However, differential expression as indicated in Figure 1 is a relative term based on the levels found in the samples analyzed. One skilled in the art readily understands that in order to use the peptide of SEQ ID NO: 1 as a biomarker for Type II diabetes, a point of reference that is critical for diagnosis with respect to the level of differential expression of the claimed peptide must be disclosed. In the absence of this critical information, it is unclear as to how one of skill in the art can reasonably determine if the peptide of SEQ ID NO: 1 can be used as a diagnostic marker for Type II diabetes. Thus, a skilled practitioner would have to resort to a substantial amount of further experimentation in order to be able to practice Applicant's invention. It is a matter of law that the claimed invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention.

The Declaration of Lander under 37 CFR 1.132 filed on February 09, 2006 has been fully considered. The Declaration is insufficient to overcome the rejection of claim 1 based upon lack of utility and enablement as set forth in the last Office action because: the Declaration presents copies of Figures 1-4, as originally filed, which are "evidence of record" which supports Applicants' possession of the claimed peptides (SEQ ID NOS:1 and 4) and their relationship to Type 11 diabetes". However, the Examiner does not doubt or dispute the results of differential expression of the instant claimed peptides of SEQ ID NO: 1 and 4. The main point of disagreement appears to be the interpretation of these results and what constitutes a specific and

substantial credible utility. The Examiner maintains that practical utility of the instant claimed peptides of SEQ ID NO: 1 and SEQ ID NO: 4 cannot be simply extrapolated from the data limited to its differential expression. A significant further research is required to identify or reasonably confirm a "real world" context of use of the claimed protein, see *Brenner v. Manson.*

At page 30 of the Response, Applicant submits that because the instant specification shows differential expression of biopolymer markers of SEQ ID NO: 1 and 4 between Type II diabetes and normal healthy control, "one of skill in the art would recognize differentially expressed peptides to be potential markers for a disease condition". It appears that Applicant has taken the position that disclosure of data limited to analysis of two groups of protein samples (disease *vs.* control) is sufficient to support the utility requirement under 35 U.S.C. 101. However, one skilled in the art readily appreciates that many proteins are differentially expressed between healthy and "diseased" tissues (cancer cells, for example, overexpress a plurality of proteins by virtue of uncontrolled proliferation); however, not all of these proteins constitute biomarkers, as molecules that allow to distinguish disease *vs.* healthy state.

The Examiner fully agrees that identification and selection of reliable biomarkers to diagnose pathological conditions is a known practice (pages 27-30). Moreover, identification of a marker that is specifically associated with a particular condition (present/absent or present at specific altered levels as compared to normal control) constitutes a specific and substantial credible utility even if a biological role of the molecule itself is not known or disclosed. However, this is not a factual situation here. In the instant case, Applicant's invention is predicated on the finding that samples of blood taken from patients with Type II diabetes contain proteins in the forms and amounts that are different from normal control samples. Applicant

further extrapolates this result into a diagnostic tool for Type II diabetes. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine the level of differential expression of peptide of SEQ ID NO: 1 that is diagnostic of Type II diabetes, and then to assay if the peptide could be used to diagnose Type II diabetes, as well as to treat Type II diabetes.

At pages 22-23 and 24-25, Applicant argues that finding biomarkers that are linked with a disease through differential expression is a common practice and refers to two publications (Patterson and Weinberg). Regarding the merit of the argument, there appears to be no evidence presented in Applicant's cited articles that would support a conclusion that any protein that is found to be differentially expressed under a pathological condition, could be immediately used as a marker for that condition. It is obvious to expect that many proteins are differentially expressed during the course of Type II diabetes; however, not all of them can serve as diagnostic biomarkers. One skilled in the art readily appreciates that detection of differentially expressed proteins represents only the first step in identification of molecules that have a diagnostic potential. The search for a diagnostic marker is usually divided into two steps; the first step being an exploratory search to identify a subset of proteins that may be involved in physiological/pathological process and the second step, which involves a very focused research to confirm that the detected differentially expressed protein could be used as a marker. The instant specification identified a peptide that is differentially expressed between Type II diabetes samples and normal control. However, there appears no further characterization presented that would lead to the "real world" specific utility of this peptide as biomarker for Type II diabetes. There is little doubt that, after complete characterization, these peptides of SEQ ID NO: 1 and

SEQ ID NO: 4 may be found to have a specific and substantial credible utility as a biomarker. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA. *See In re Fisher,* 2005 WL 2139421 (Sept. 7, 2005). The *Fisher* court interpreted *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility" 2005 WL 2139421, at *4. The *Fisher* court held that § 101 requires a utility that is both substantial and specific. *Id.* at *5. The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public." *Id.*

Just as in *Fisher* case where the Board reasoned that use of the claimed ESTs for the identification of polymorphisms is not a specific and substantial utility because "[w]ithout knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage," (*Id.,* slip op. at 15), in the instant case, detection of peptides of SEQ ID NO: 1 and SEQ ID NO: 4 in a sample of a patient provides no meaningful information as to the "link" or diagnosis determination. While an assay that detects the presence of a marker that has a stated correlation to a specific disease condition would be considered a "substantial utility" in the context of providing a diagnostic tool, in the instant case the claimed peptide is suitable only for further research, which constitutes a utility that is not considered a "substantial utility". See

Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility.

Finally, with respect to limitation present in claim 1, "evidences a link to Type II diabetes", the Examiner maintains that disclosure of peptides of SEQ ID NO: 1 and SEQ ID NO: 4 as being linked to a pathological condition constitutes a utility, which requires further research to identify or reasonably confirm a "real world" context of use. At present, it appears that the only information obtained from identifying the presence of a biopolymer marker of SEQ ID NO: 1 or 4 is the determination of "a link to Type II diabetes". One skilled in the art readily appreciates that many factors have a link to or are associated with a particular pathological condition. In *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), the court specifically stated that "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion". To grant Applicant a patent encompassing isolated fragments of a naturally occurring human protein, which are not readily usable in their current form, would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *Brenner v. Manson, Ibid*). To grant Applicant a patent on the claimed peptides based solely upon an assertion that the protein is linked to Type II diabetes is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted.

Thus, since the instant specification does not disclose a credible "real world" use for the isolated biopolymer markers of SEQ ID NO: 1 and SEQ ID NO: 4 in currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

7. Claim 1 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

8. No claim is allowed.

9. This application contains claims 39-46 drawn to an invention nonelected with traverse in Paper filed on March 09, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

February 22, 2006